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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,200	04/18/2005	Roberto D'Alessio	17722 (PC27004)	5147

7590 06/05/2007  
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Suite 300  
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EXAMINER
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FREISTEIN, ANDREW B

ART UNIT	PAPER NUMBER
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1626

MAIL DATE	DELIVERY MODE
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06/05/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/505,200

Applicant(s)

D'ALESSIO ET AL.

Examiner

Andrew B. Freistein

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 1-12, 23-26 and 28-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-22 and 27 is/are rejected.
- 7) ☒ Claim(s) 13-22 & 27 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

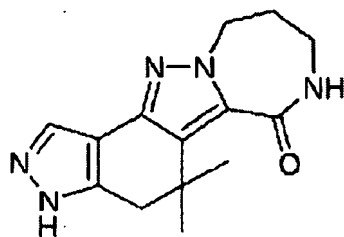
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|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

The amendment filed 4/18/2007 was entered. Claims 1-32 are pending.

#### ***Restriction Requirement***

Applicant asserts that there is a discrepancy between the elected subject matter and the examined subject matter. On page 5 of the Office Action, the scope of the elected invention is defined, which encompasses the elected species,



, additional compounds of formula (Id) and additional compounds of formula (I). The scope of the withdrawn compounds is listed on page 6 of the Office Action. The elected species was searched and the scope of the search was broadened to the extent necessary to determine patentability. Le Tourneau et al anticipate the entirety of the claims (see 35 USC 102(b) rejection below). In order to comply with the restriction requirement, claims to compounds falling outside of the elected invention must be cancelled or amended to exclude the non-elected subject matter as defined on page 6 of the last Office Action.

#### ***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-22 are 27-rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention, because of the term, "hydrido." As a result of the amendment filed 4/18/2007, this rejection is withdrawn.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of the formula (I), isomers, tautomers, carriers and pharmaceutically acceptable salts thereof, the specification does not reasonably provide enablement for prodrugs of compounds of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is maintained and made FINAL.

Applicant traverses the rejection asserting that, "it is well understood in the art tha that the term "prodrug" refers to a precursor of a drug, i.e. a compound, that, on administration, undergoes chemical conversion by metabolic processes before becoming an active pharmacological agent."

The rejection is maintained. Examiner agrees that one of ordinary skill in the art knows the meaning of the term "prodrug" (a definition of the term "prodrug" is provided in the Office Action at page 8). However, the rejection is maintained, because the instant specification does not enable one of ordinary skill in the art to make a prodrug of

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a compound of formula (I). This is an enablement rejection (35 USC 112, 1<sup>st</sup> paragraph) rather than an indefiniteness rejection (35 USC 112, 2<sup>nd</sup> paragraph).

In the instant case, the specification fails to provide the mechanism of action for producing a prodrug of a compound of formula (I). Providing the definition of a prodrug without enabling a skilled artisan how to make a prodrug is not sufficient. The only guidance provided in the specification is for the preparation of compound of formula (I) and pharmaceutically acceptable salts. Thus, in order to overcome this rejection, the term "prodrugs" must be deleted.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

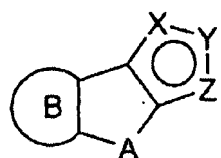
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-18 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Le Tourneau et al., US Pat. No. 4,734,430. This rejection is maintained and made FINAL.

Applicant traverses the rejection by stating that the elected species is novel over the prior art and that it is encompassed in the elected subject matter. Whether the species is novel over the art is irrelevant to the rejection of these claims. The claims are anticipated. Currently, claims 13-18 and 27 are drawn to compounds that are anticipated by Le Tourneau et al. In order to overcome this rejection, the claims must be either cancelled all together or amended in order to overcome the rejection.

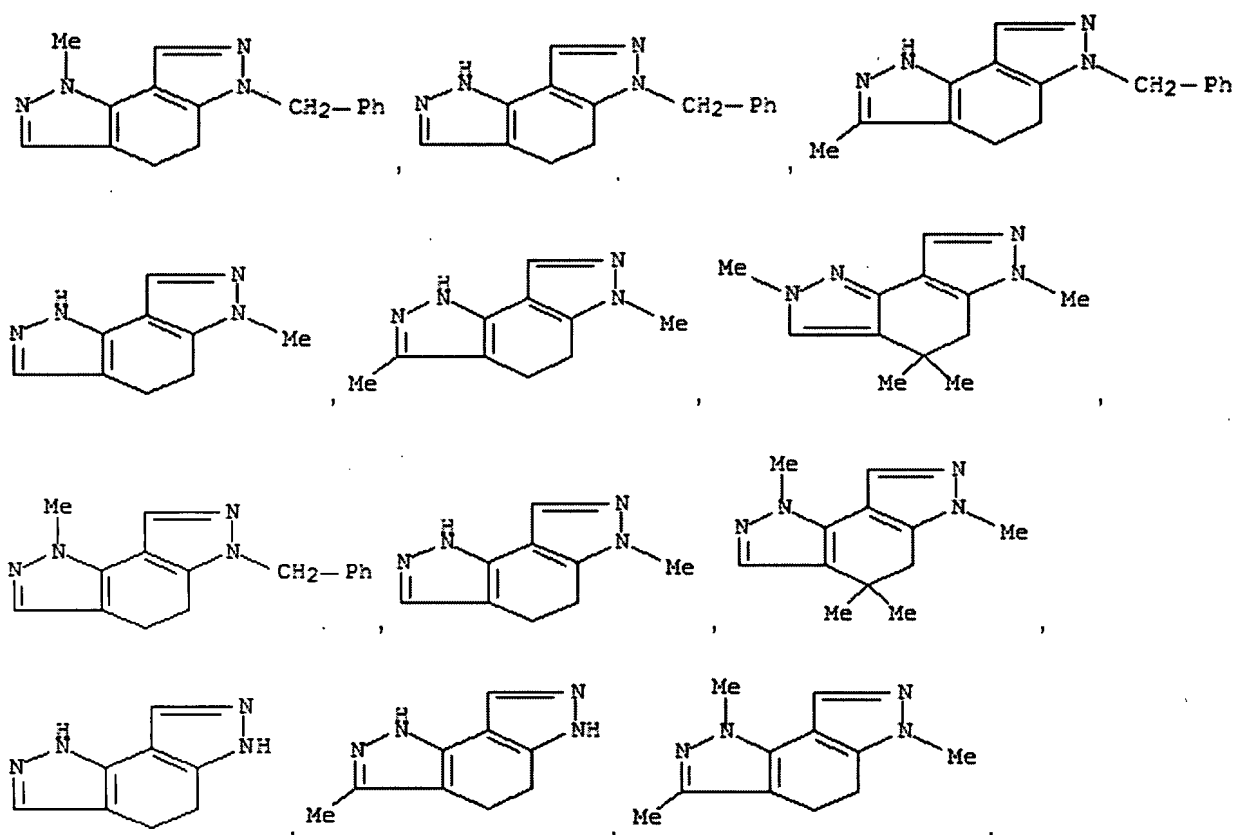
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Claims 13-18 of the instant application is drawn to a compound of formula (I),

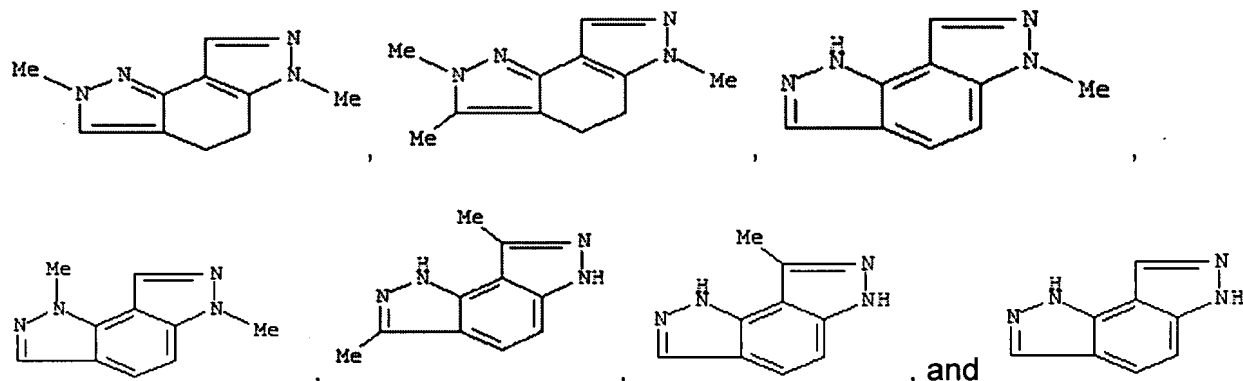


, wherein X is  $\text{CR}_1$ ;  $\text{R}_1$  is hydrogen or lower alkyl; Y is N; Z is  $\text{NR}_1$ ; A is  $(\text{CH}_2)_m$  or  $(\text{CR}_z\text{R}_y)_p$ ; m is 2;  $\text{R}_z$  is hydrogen;  $\text{R}_y$  is hydrogen; p is 2; B is a 5-membered aromatic ring having 0 to 3 heteroatoms selected from S, O and N; each of X, Y, Z and B rings are optionally further substituted with one or more L- $\text{R}_2$  groups; L is a single bond or an alkylidene group; and  $\text{R}_2$  is hydrogen, alkyl, or a 5-12 membered monocyclic ring having 0-3 heteroatoms.

Le Tourneau et al., US Pat. No. 4,734,430 discloses the compounds



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(see Le Tourneau, STN International, HCAPLUS Database, Columbus, OH, Accession No. 1988:454772, Reg. Nos. 115309-93-8, 115309-94-9, 115309-95-0, 115309-98-3, 115309-97-2, 115309-92-7, 115310-00-4, 115310-01-5, 115310-05-9, 115310-12-8, 115310-06-0, 115310-07-1, 115310-09-3, 115310-10-6 and 115310-11-7 (2007)).

Additionally, Le Tourneau et al. disclose pharmaceutically acceptable acid addition salts of the compounds and pharmaceutical compositions comprising the compounds (see US 4,737,430, col. 1, lines 40-61 and col. 5, lines 9-58).

Again, in order to overcome this rejection, the claims must be (1) cancelled all together or (2) amended in order to overcome the rejection.

### ***Claim Objections***

Claims 13-22 and 27 are objected to as being drawn to non-elected subject matter.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M<sup>c</sup>Kane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein  
Patent Examiner, AU 1626



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Joseph K. M<sup>c</sup>Kane  
Supervisory Patent Examiner, AU 1626  
Date: May 30, 2007